

# The illnesses of Carlo di Ferdinando I de' Medici: a second opinion

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## Abstract

### Objectives

*To offer a second opinion on the recently published retrospective diagnosis of Cardinal Carlo de' Medici (1596–1666), a prominent member of the grand ducal family then ruling Tuscany.*

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### Methods

*Retrospective diagnosis of historical figures is difficult and at times controversial, even with modern technology. It is based on contemporaneous medical descriptions and historical reviews, inherited iconography, and rarely – as in the case of the Medici of Florence – skeletal assessment, completed with radiological, histological and even immunological studies. Modern clinical work is often complemented with a second opinion obtained from specialists in the relevant fields. It is this type of second opinion that our collaborative Australian and Italian team, comprised of an orthopaedic/spinal surgeon, a rheumatologist and two medical historians, now offers.*

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### Results

*The authors concur with the first opinion's diagnosis of Klippel-Feil syndrome in Carlo de' Medici, but disagree with the diagnoses of tuberculosis (Pott's disease) and rheumatoid arthritis. We find evidence, instead, for a psoriatic-DISH arthropathy with involvement of Klippel-Feil syndrome.*

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### Conclusions

*A psoriatic-DISH arthropathy, previously described by the present authors as the 'Medici syndrome', was commonly found in the males of the primary branch of the family. The diagnosis of this condition in Cardinal Carlo de' Medici represents its first identification in a male of the secondary (grand ducal) branch of the family.*

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### Key words

Carlo de' Medici, medical history, skeletal pathology, radiology, diagnosis

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## Introduction

The medical history of Cardinal Carlo de' Medici (19.3.1596 to 17.6.1666) was recently published in a detailed description, presenting a well-argued diagnosis (1). This first opinion frequently quotes Pieraccini's earlier study, which makes reference to Carlo's spinal conditions. Not quoted, however, is the information on the child's maturation: namely "when aged 4 or 5, [he was] a child small in physical development, less active in early years, somewhat slow in intellectual development" (2, p. 425). His condition changed during the years to come since, by the age of 20, Carlo was intellectually well-developed and was sent to Rome to receive his red cardinal's hat. He became active in hunting, celebrations and music. His physical development was influenced by several infections, spinal anomalies and various other symptoms.

Our second opinion is based on contemporaneous data preserved in a variety of archival collections (3-5). Our opinion is also based on the work of Pieraccini, and on publications arising from the Progetto Medici team (6-12). The conclusions reached in the published *primary diagnosis* on Carlo's illnesses are far reaching. Our team, however, has arrived at a different opinion on some aspects of this diagnosis.

First, however, we suggest a clarification of the family branch to which Carlo belonged. The *primary opinion* stated that Carlo's line "began with Giovanni delle Bande Nere (1498-1526), a famous captain of mercenary troops, and ended with Gian Gastone (1671-1737), the last Medici grand duke" (1, p. 595). While Giovanni della Bande Nere was the father of the first of the Medici grand dukes, Cosimo I (1519-1574), the branch of the family to which both Giovanni delle Bande Nere and the subsequent grand dukes belonged started a century earlier with Lorenzo di Giovanni di Bicci in 1395. And although Gian Gastone was the last of the grand dukes, his sister Anna Maria Lodovica outlived him, ending the family line in 1743 (13).

More importantly than the above matter of historical detail, we suggest the

following interpretations of the spinal, cutaneous, and peripheral articular illnesses of Carlo.

## Analysis of the first opinion, namely of a detailed description of Carlo's illnesses, given in a previous article (1)

### Spinal anomalies

The first opinion suggests that Carlo suffered from congenital Klippel-Feil syndrome with multiple variations in vertebral segmentation, and classified his condition as grade III, with the "skull fused to the cervical spine". This diagnosis meets with our agreement, but with certain qualifications, as indicated below.

### Skull

The first opinion reported "total atlanto-occipital fusion" (AOF). Although there are no photographs or radiological images presented, the fusion is plausible. In our second interpretation, we note that the CT presented with no visible occipital condyle on the separated skull (Fig. 1). The CT also indicates a probable platybasia, measured on lateral skull x-ray, with 143 degree angle between the horizontal line (nasion and centre of pituitary fossa) and an oblique/vertical line between centre of pituitary and foramen magnum (normal 125-143 degrees). The margins of the foramen magnum are smooth, the diameters are wide. One remains puzzled about the mechanism of separation of the AOF, was it accidental, or was it intentionally done after the exhumation?

### Cervical spine

The apical image of the C1 (seen in a photograph), showed a wide spinal canal with smooth margins. Of particular interest is the sagittal CT image of the cervical spine (with one slice only and with no specification of the position of the cut), presumably in the centre of the vertebra. The C6-7 inter-body fusion is obvious: C6 is wedge shaped, assessed in the first opinion, as "typical of tuberculosis". A less evident wedge deformity, not mentioned in the first opinion, is also present at C7 vertebral level, slightly clouded by the anterior and posterior osteophytes. (Fig. 2A-B).

Competing interests: none declared.



**Fig. 1.** Carlo's CT scan: base of skull. (With permission of the Soprintendenza Ministero per i Beni e Attività Culturali, Firenze, 26 ottobre 2010)

#### *Alignment of the cervical column*

The wedged C6 is with 30% compression and the C7 vertebra with 15% compression. Nevertheless (measured with Cobb method) the lordotic curvature is maintained at C1-5, with sudden kyphotic angulation at C6 of 20 degrees, not sufficient however for externally detectable gibbus, probably the positive result of applying the metal brace ("iron corset"), provided for Carlo by the Padovan physician Girolamo Fabrizio d'Acquapendente (1537–1619) (14, p. 174).

#### *Osteoporosis and degenerative changes*

All vertebral bodies are porotic, but with solid surrounding cortex. Calcification of the C2-3 anterior longitudinal ligament (ALL) is seen on the lateral x-ray views. There are degenerative osteophytes at the lower C5, upper C6/C7 levels, and sclerotic changes at the upper endplate of C6. These are reactive changes resulting either from infection,

or more likely from trauma, as no similar reactive changes are seen above the C5 level.

#### *Thoracic and lumbar variations*

The *gibbus deformity* mentioned as cervical in the primary opinion is in the upper thoracic level, according to Pieraccini (2, pp. 422, 424).

The description of these variations is valid. Of particular interest in our view would be the calcification of the anterior longitudinal ligament (ALL), which is reported but not exhibited. Is it a full width ossification or only a hemi-ossification of the ligament? Of significance also is the unilateral sacro-iliac (S-I) fusion.

#### *Tuberculous "neck fistula" (1, p. 599)*

The term "fistula" could not be found in the quoted sources. A more appropriate term would be "scrofula", a discharge, caseous in the case of TB, originating in a subcutaneous lymph node in the neck. The lymph nodes have no com-

munication with the vertebral bodies, as might be construed from the text.

A chronic tuberculous discharge would have multiple openings, leaving hypertrophic, keloid scars (15). No such post-scrofula scarring was ever mentioned in the contemporary narratives on Carlo.

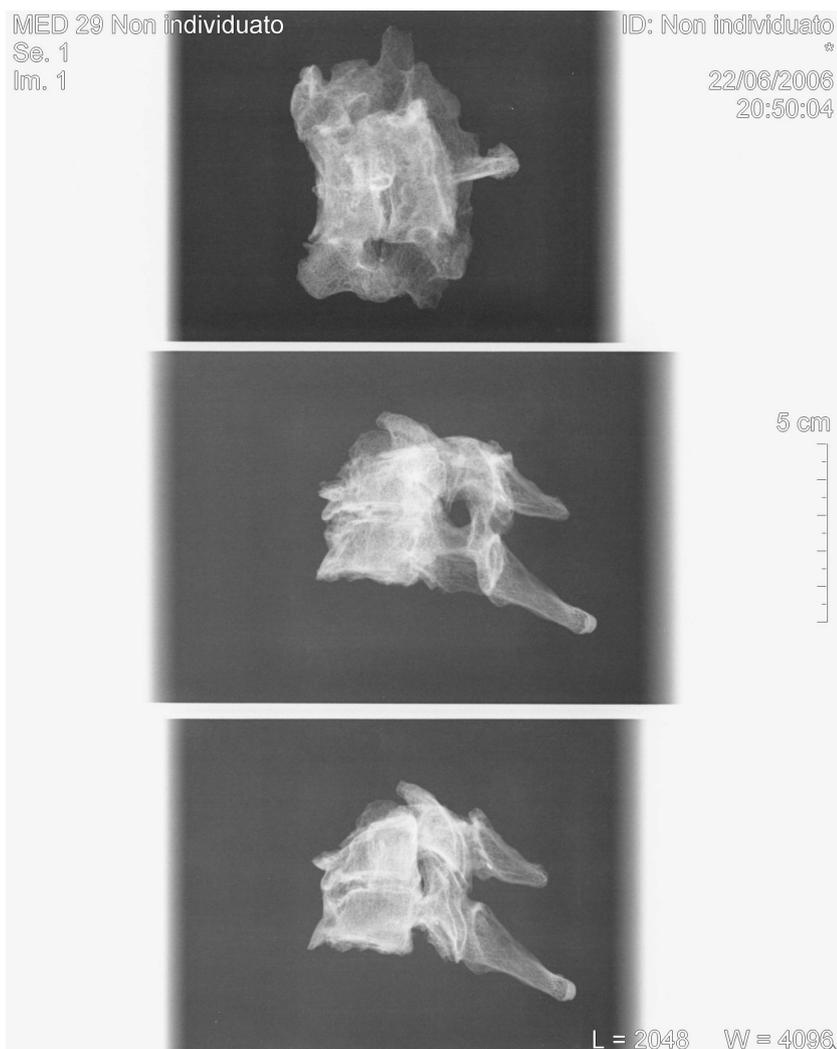
#### *Vertebral tuberculous osteomyelitis*

In radiology, a TB infection of the body of the vertebra is diagnosed by the image of "spreading out" (Fig. 2). The infection erodes the cortex of the vertebral body and the "lateral expansion" becomes somewhat typical of granulomatous osteomyelitis of the vertebrae. Such collections could be reabsorbed, in which case healing emerges with rounded, calcified lateral ligaments, but these are not recognisable in Carlo's presented radiological images. In our opinion there is no definite radiological sign of vertebral tuberculous osteomyelitis in Carlo de' Medici.

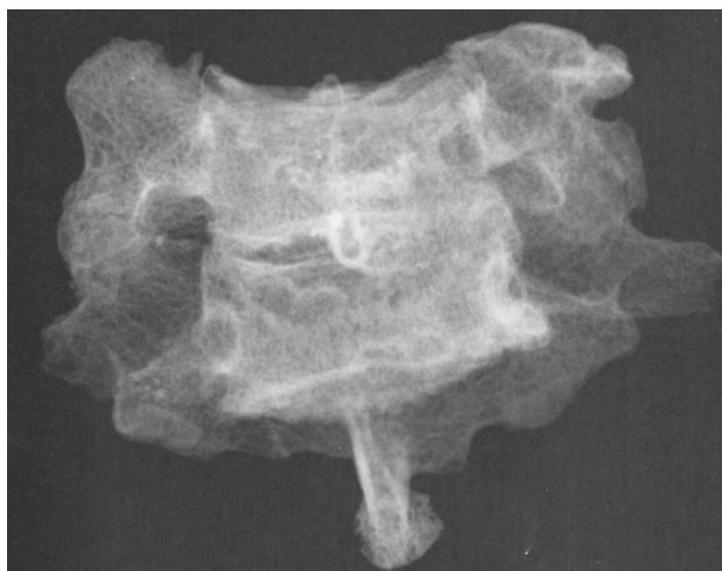
#### *Osteolysis*

The single osteolytic area in the middle of the wedged C6, described by the first authors, is not typical of any specific disease (15-19). In Carlo's case, the vertebral body has a solid cortex but porous matrix: it could be metastatic, infectious or metabolic. The bone density was not measured for differentiation, which would have been feasible on the CT; the published radiological findings are therefore controversial.

Our conclusive second opinion on Carlo de' Medici's possible TB is as follows: with the subject having no episodes of haemorrhagic coughing along the years, being non-cachectic, showing a normal vertebral cortex, with wedge deformity of two vertebral bodies, but with no parallel transverse diameter widening or lateral para-vertebral ligament calcification, the diagnosis of TB is not sustainable. Although remission from vertebral osteomyelitis is possible, long term survival in the seventeenth century would have been unlikely. The subcutaneous submentorial discharge could have resulted from a frequently mentioned dental abscess from which Carlo suffered, arising from a double tooth deformity that was eventually cured by extraction (4, 5).



**Fig. 2A.** Carlo's cervical spine, lateral views at C5-6 level. Note wedged C6 and less so C7. (With permission of the Soprintendenza.)



**Fig. 2B.** AP views of last two cervical vertebrae. Note equal transverse diameter of the two vertebrae, with no para-vertebral calcifications. (With permission of the Soprintendenza.)

#### Cutaneous conditions

In response to the primary authors' statement, referencing Pieraccini, that "in the chronicles of the cardinal's life conserved in the Florentine archives, no mention of any dermatological problems can be found" (1, p. 601), our second opinion is different. Pieraccini includes reports of "rogna" for the 25th of April, 1620 ("febbre ...finissima roгна") and the 2nd of May, 1620 ("il cardinale se ne sta con la sua roгна") (2). Several other references to Cardinal Carlo's skin disorders along the years are recorded in the archives: "rottura di pelle", "resipola", "grattatura" in the years 1601, 1644, 1654 and 1655 (4, 5). Although in today's nomenclature these descriptions would not be characteristic, they are signs of recurrent skin erythemata. The definition of "rogna" therefore is essential: this skin disorder is described as an erythematous condition, an eczema encountered over unspecified areas of the body, often associated with pruritus (20, 21). These antiquated definitions are updated by Pieraccini himself as "eczema pruriginosa" (2), and by the recent Oxford Dictionary interpretation (2004) in which "rogna" is a crust on the skin.

#### Peripheral conditions

The first authors' diagnosis of the joint disease in Carlo's extremities was reached by applying an eliminatory differential diagnosis. The authors found the differentiating process between rheumatoid (RA) and psoriatic (PsA) arthritis to be the most difficult (1, p. 600). Indeed, both entities have overlapping symptoms and signs.

A definite primary diagnosis of RA was made on Carlo's skeleton, on the basis of "the symmetrical and polyarticular features of the disease, the specific joints involved [that is, the carpal, metacarpo-phalangeal (MP) and proximal inter-phalangeal (PIP) joints], and the swan-neck deformity in both hands" (1, p. 600).

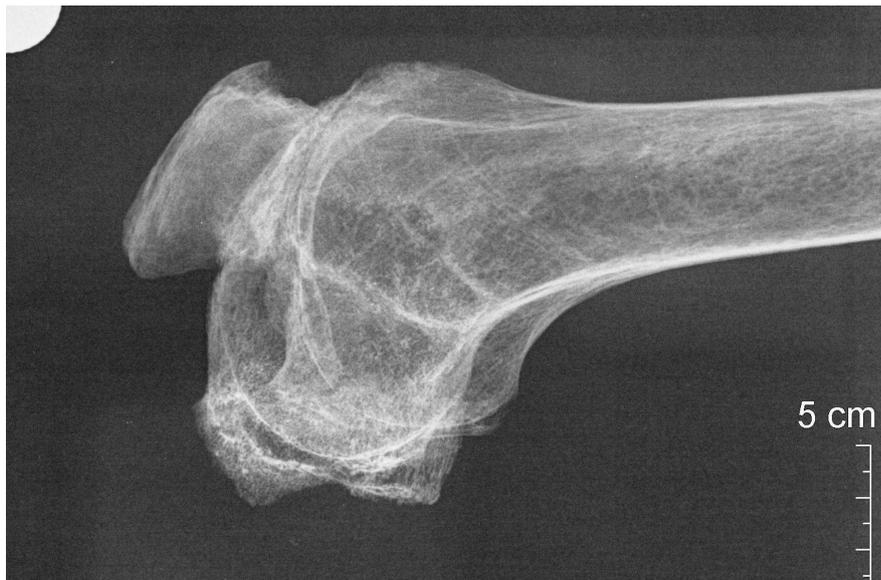
Our second opinion disputes this diagnosis based on what is considered to be the "gold standard" for the radiological diagnosis of RA (22, 23). We could find no definite subchondral erosions in the images presented by the first authors or



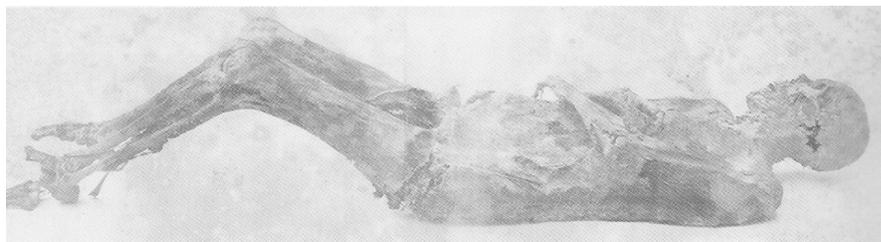
**Fig. 3A.** Carlo's finger x-ray: with metacarpal bones, flexed proximal interphalangeal joint, and missing distal phalanxes. (With permission of the Soprintendenza).



**Fig 3B.** A personal schematic representation of Boutonnière's deformity (proximal, middle and distal phalanxes).



**Fig. 4A.** Carlo's x-ray of knee: flexed ankylosis.(with permission of the Soprintendenza)



**Fig. 4B.** Skeleton x-ray of Piero il Gottoso with flexed knees. (Reprinted with permission).

in the additional ones that we obtained from the Archives. The osteoporosis, probably a result of prolonged inactivity, is mild and diffuse rather than only subchondral, with no presence of subchondral cysts, and no ulnar deviations of fingers at MP joint level. We found the joint surfaces intact rather than destroyed, ankylosis was mainly by bony excesses, with no mal-alignment and therefore in our view, not diagnostic of RA (24, 25).

For our assessment we adopted Larsen's grading in which ankylosis, the last out of five grades in RA, is present only following destruction of joint surfaces (26). Based on the diagnostic criteria for RA given by the American College of Rheumatologists (1987) and the European League Against Rheumatism (EULAR) (27-29), we cannot accept the diagnosis of RA.

Finally, with regard to swan neck deformity, the first opinion presented it as a finger deformity "typical in RA" (1, p. 599), this being a hyperextension of

the PIP joints and a flexion of the distal interphalangeal joints (DIP). The published image in the article is presented as "a flexed PIP and nonexistent distal phalanx". If diagnosed despite the missing phalanx, it would correspond to Boutonnière's deformity rather than to a swan neck deformity (25, pp. 216-7). (Fig. 3A-B).

*An alternative diagnosis*

The authors of this second opinion offer an alternative diagnosis of Carlo's skeleton, incorporating a triple pathology, namely a combined *Psoriatic-DISH arthropathy*. The components of this pathology are:

1. The *Psoriatic* diagnosis follows the grading of CASPAR, the classification introduced by an International team of Academics in 2006, and accepted by the EULAR in 2008 (30). It carries a sensitivity of 91.4% and a specificity of 98.7%. The scoring system requires a total of three points accumulated from symptoms: presence of psoriasis (2

points), family history of psoriasis (1 point), dactylitis (1 point) and juxta-articular bone formation (1 point). Using the CASPAR classification, Carlo's condition scored 4 points on the basis of cutaneous, peripheral arthropathy and unilateral sacro-iliac involvement (31, 32).

2. A congenital Klippel-Feil syndrome.  
3. Acquired degenerative pathology, namely calcification of the anterior longitudinal ligament (ALL), both cervical and thoracic, indicating diffuse idiopathic systemic hyperostosis (DISH). These conditions, taken together with Carlo's cutaneous and joint pathologies indicated above, correspond to the "Medici syndrome", previously detected in the male members of the primary branch of the family (33). This combined pathology of psoriasis and DISH syndrome was rarely encountered in the medical or paleopathological literature, especially before the nineteenth century when rheumatoid arthritis was defined as a separate entity (34). The peripheral arthropathy involves ankylosis: the knee deformities are in flexion without subluxation or chondral erosions (Fig. 4A). This condition is similar to that of Carlo's collateral ancestor some 150 years earlier, Piero il Gottoso (1416-1469), and it was already described as Forestier's disease by Costa and Weber (Fig. 4B) (35).

## Conclusion

Carlo di Fernando de' Medici – cardinal, intellectual and supporter of the arts – was plagued by congenital and acquired degenerative and autoimmune diseases. The authors have analysed the published primary diagnosis and whilst agreeing with part of it, have objected to the final diagnosis of rheumatoid arthritis. In a detailed description, illustrated with newly obtained radiological images and with the contemporaneous medical descriptions of a skin disorder, the authors conclude that Carlo suffered from a combined psoriatic arthropathy with DISH features. This combined diagnosis, previously presented as the "Medici syndrome" (33) was frequent in the primary line of the Medici family and may have contributed to its early extinction (36). It is now also diagnosed

in the case of a prominent member of the family's secondary line, Carlo di Ferdinando.

## References

- GIUFFRÀ V, VITTIELLO A, GIUSIANI S *et al.*: Rheumatoid arthritis, Klippel-Feil syndrome and Pott's disease in Cardinal Carlo de' Medici (1595-1666). *Clin Exp Rheumatol* 2009; 27: 594-602.
- PIERACCINI G: La Stirpe de' Medici di Caffaggiolo: Saggio di ricerca sulla trasmissione ereditaria dei caratteri biologici. Nardini Editore. Firenze. 1986 [reprint; first published 1924-25]. Vol. II. pp. 411-31.
- Medici Archives Project ([www.medici.org](http://www.medici.org)) 2005.
- Miscellaneous Medici Archives.
- Mediceo del Principiato, Asf. Mdp. 5985 MDP 113, 114.
- FORNACIARI G, VITIELLO A, GIUSIANI S, GIUFFRÀ V, FORNACIARI A, VILLARIN: The Medici project: first anthropological and paleopathological results of the exploration of the Medici tombs in Florence. *Med Secoli* 2007; 19: 521-43.
- FORNACIARI G: Il "Progetto Medici": Studio antropologico e paleopatologico dei Granduchi. 2007. <http://www.paleopatologia.it/articoli/articolo.php?recordID=21>.
- FORNACIARI G, GIUFFRÀ V *et al.*: Autopsy and embalming of the Medici Grand Dukes of Florence (16<sup>th</sup>-18<sup>th</sup> centuries). 2008. <http://www.paleopatologia.it/articoli/articolo.php?recordID=36>.
- FORNACIARI G: Le malattie reumatiche alla corte medicea di Firenze: la cosiddetta "gotta" dei Medici. 2009. <http://www.paleopatologia.it/articoli/articolo.php?recordID=143>.
- FORNACIARI G, GIUFFRÀ V: La malattia reumatiche alla corte medicea di Firenze: La cosiddetta "gotta" dei Medici. *Reumatismo* 2009; 61: 229-37.
- VILLARIN, FORNACIARI G *et al.*: Scenes from the Past. The Medici Project: Radiographic Survey. *Radiographics* 2009; 29: 2101-14.
- GIUFFRÀ V, VITIELLO A, GIUSIANI S *et al.*: Spinal Pathology in the Medici Family, Grand Dukes of Florence (XVI-XVII Centuries). *Paleopathology Newsletter* no. 2010; 150: 24-33.
- CATALIOTTI L, LIPPI D, LOTTI T: Dermographism: the illness and death of Anna Maria Lodovica de' Medici, Palatine Electress (1667-1743). *Dermatol Ther* 2010; 23 (Suppl. 2): S37-S40.
- FABRIZI D'ACQUAPENDENTE G: Opere chirurgiche. G. Cadorino. Padova. 1685.
- SLATER RR, BEALE RT, BULLIT E: Pott's disease of the cervical spine. *Southern Med J* 1991; 84: 521-32.
- LABERGE JM, BRANDT-ZAWADSKI M: Evaluation of Pott's disease with computed tomography. *Neuroradiology* 1984; 26: 429-34.
- WURTZ R, QUADER Z, SIMON D, LANGER B: Cervical Tuberculous Vertebral Osteomyelitis: Case report and discussion of literature. *Clin Infect Diseases* 1993; 16: 806-8.
- LOEMBE PM: Tuberculosis of the lower cervical spine (C3-7) in adults: Diagnostic and surgical aspects. *Acta Neurochir (Wein)* 1994; 131: 125-9.
- MOORTHY S, PRABHU N: Spectrum of MR Imaging findings in Spinal Tuberculosis. *Amer J Roentgenol* 2000; 179: 979-83.
- MARCOVECCIO E: Dizionario etimologico storico dei termini medici. Festina Lente. Firenze. 1993.
- BARETTI GMA: A Dictionary of the English and Italian languages. Richardson. London. 1760.
- VAN DER HEIJDE DM: Radiographic imaging: the "gold" standard for assessment of disease progression in rheumatoid arthritis. *Rheumatology* 2000; 39 (Suppl. 1): 9-16.
- VAN DER HEIJDE DM, LEEUWEN MA, KOSTER AM *et al.*: Biannual radiographic assessments (hands and feet) in a three-year prospective follow up of patients with early rheumatoid arthritis. *Arthritis Rheum* 1992; 35: 26-34.
- FUCHS HA, KAYE JJ, CALLAHAN LF *et al.*: Evidence of significant radiographic damage in rheumatoid arthritis within the first two years of disease. *J Rheumatol* 1989; 16: 585-91.
- RESNICK D, KRANSDORF MI: Bone and Joint Imaging: rheumatoid arthritis and related diseases. Third ed. Elsevier Saunders. New York. 2007, pp. 210, 234-37, 576.
- LARSEN A, DALE K, EEK M: Radiographic evaluation of rheumatoid arthritis and related conditions by standard reference films. *Acta Radiol Diagn* 1997; 18: 481-91.
- ARNET FA, EDWORTHY SM, BLOCH DA *et al.*: The American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis. *Arthritis Rheum* 1988; 31: 315-24.
- VAN GESTEL AM, PREVOO ML, VAN HOF MA *et al.*: Development and validation of the EULAR response criteria for rheumatoid arthritis. *Arthritis Rheum* 1998; 41: 942-5.
- VAN GESTEL AM, ANDERSON JJ, VAN RIEL PL *et al.*: ACR and EULAR improvement criteria have comparable validity in rheumatoid arthritis trials. *J Rheumatol* 1999; 26: 705-11.
- KHAN MA: Psoriatic arthritis: an update from EULAR 2007, from the Annual European Congress of Rheumatology. *Medscape*, May 2008.
- TAYLOR W, GLADMAN D, HELLIWELL P *et al.*: Classification Criteria for Psoriatic Arthritis. Development of new criteria from a large international study. *Arthritis Rheum* 2006; 54: 2665-73.
- SLOBODIN G, ROSNER I, ROZENBAUM M *et al.*: Psoriatic arthropathy: where now? *IMAJ* 2009; 11: 430-4.
- WEISZ GM, MATUCCI-CERINIC M, ALBURY WR, LIPPI D: The Medici syndrome, a medico-historical puzzle. *Intern J Rheumatic Dis* 2010; 13: 125-31.
- TANIGUCHI T, MAEJIMA H, WATARAI A, AKI R, KATSUOKA K: A case of psoriasis with diffuse idiopathic skeletal hyperostosis involved with ossifications of posterior and anterior longitudinal ligament. *Rheumatology Int* 2010. DOI: 10.1007/s 00296-010-1368-7.
- COSTA A, WEBER G: Le alterazioni morbose del sistema scheletrico in Cosimo dei Medici il Vecchio, in Piero il Gottoso, in Lorenzo il Magnifico, in Giuliano Duca di Nemours. *Arch de Vecchi Anat Patol* 1955; 23: 1-39.
- LIPPI D, MATUCCI-CERINIC M, ALBURY WR, WEISZ GM: Longevity and causes of death of adult males in the Medici di Bicci family. *J Family Hist* 2009; 34: 243-50.